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AWARD NUMBER: W81XWH-15-1-0094

TITLE: TBI Assessment of Readiness Using a Gait Evaluation Test
(TARGET): Development of a Portable mTBI Screening Device

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14. ABSTRACT With up to 320,000 service members sustaining some form of traumatic brain injury (TBI) over the past 14 years, the lack of an objective measurement tool for evaluation and monitoring of TBI is of great concern to the military. The NeuroCom® Sensory Organization Test (SOT) is the current 'gold standard' for assessing mTBI-related motor impairments. However, the equipment's size and logistical footprint makes it impractical for field deployment. This study seeks to determine the validity and reliability of an Android device-based mTBI (mild traumatic brain injury) screening test app for assessing motor function. The app, AccWalker, utilizes the smartphone's accelerometer and orientation metrics in order to assess a person's functional motor ability. The study will seek to establish test-retest and inter-rater reliability of the app within a healthy civilian population, concurrent validity with the SOT, BESS, CB&M test (three currently used assessments) in a healthy civilian population, and predictive validity to discriminate between healthy individuals and those with clinically confirmed mTBI in both a civilian and military population.					
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1. INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.

With up to 320,000 service members sustaining some form of traumatic brain injury (TBI) over the past 14 years, the lack of an objective measurement tool for evaluation and monitoring of TBI is of great concern to the military. The NeuroCom® Sensory Organization Test (SOT) is the current ‘gold standard’ for assessing mTBI-related motor impairments. However, the equipment’s size and logistical footprint makes it impractical for field deployment. This study seeks to determine the validity and reliability of an Android device-based mTBI (mild traumatic brain injury) screening test app for assessing motor function. The app, AccWalker, utilizes the smartphone’s accelerometer and orientation metrics in order to assess a person’s functional motor ability. The study will seek to establish test-retest and inter-rater reliability of the app within a healthy civilian population, concurrent validity with the SOT, BESS, CB&M test (three currently used assessments) in a healthy civilian population, and predictive validity to discriminate between healthy individuals and those with clinically confirmed mTBI in both a civilian and military population.

2. KEYWORDS: Provide a brief list of keywords (limit to 20 words).

mild traumatic brain injury (mTBI), concussion, AccWalker, Sensory Organization Test (SOT), Balance Error Scoring System (BESS), Community Balance & Mobility Scale (CB&M), Military Acute Concussion Evaluation (MACE), smartphone, TARGET, military, civilian, validity, reliability

3. ACCOMPLISHMENTS: The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction.

What were the major goals of the project?

List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

- Pre-task – Institutional Review Board and Human Research Protection Office Application, timeline: 1-2 months
 - Milestone: IRB and HRPO approval will be obtained at UNCG, 100%, completion date: 04/22/2016
 - Milestone: IRB and HRPO approval will be obtained at Temple, 100%, completion date: 04/22/2016
 - Milestone: IRB and HRPO approval will be obtained at NICoE, 25%
- Major Task 1 – Normative data collection on healthy civilians, timeline: 3-9 months
 - Milestone: 100 healthy civilians will complete the TARGET, MACE, NeuroCom’s SOT, and the Balance Error Scoring System (BESS), which will serve as our normative data
 - UNCG, 5%
 - Temple, 0%
- Major Task 2 – mTBI data collection on civilians, timeline: 3-9 months
 - Milestone: 50 civilians with mTBI will complete the TARGET, MACE, NeuroCom’s SOT, and BESS
 - UNCG, 0%
 - Temple, 0%
- Major Task 3 – Derive normative military values from previously collected data, timeline: 9-15 months
 - Milestone: data from 25 healthy military personnel who previously completed the TARGET for a separate project will be analyzed to derive military-specific norm references for reliable change index calculations
 - Percent complete: 100%
 - Although only 25 military personnel were included in the SOW, data from 90 military personnel were analyzed and reported in a recent manuscript (under review, Appendix A)
- Major Task 4 – mTBI data collection on military personnel, timeline: 15-21 months
 - Milestone: 25 military personnel with mTBI from NICoE will complete the TARGET to determine the clinical utility of the TARGET as an mTBI screen in military populations
 - Percent complete: 0%
- Major Task 5 – data analysis/software optimization, timeline: 17-24 months
 - Milestone: RCI and ROC curves will be calculated on a number of different variability metrics, 0%
 - Milestone: Optimized AccWalker that provides a simple red light indicator when neurological impairment from mTBI is detected in the stepping-in-place task, 0%

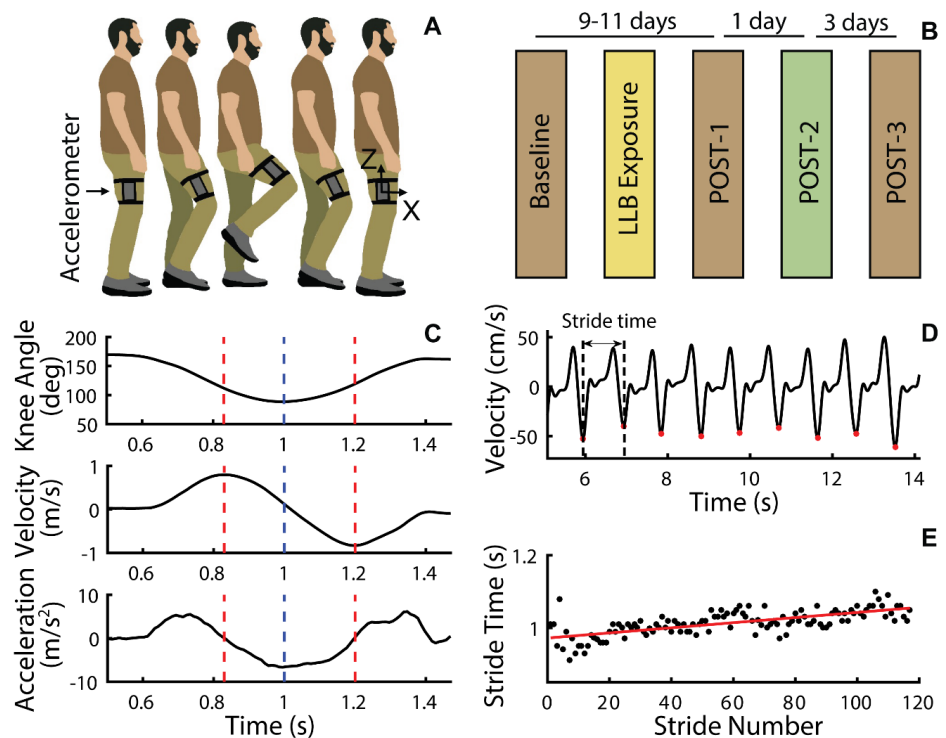
What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

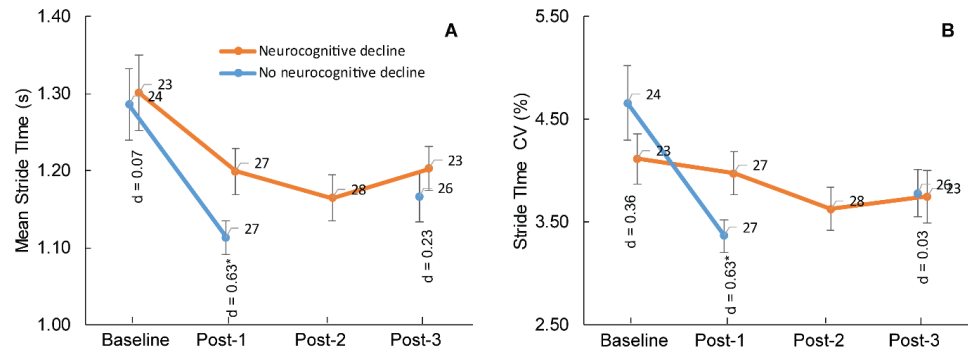
• **General Overview of Progress:**

- **May-October 2015:** Study team assembly/training and initial IRB preparation/submission
 - Relative to both sites (UNCG & Temple), several delays have occurred in Year 1.
 - Delayed assembly of study team
 - May-July 2015: The required application and interview process delayed the start of several key study team members by several months. Therefore, we were unable to hire our project coordinator and post-doc at UNCG until mid-August 2015 and our Temple post-doc until October 2015
 - Delays in IRB and HRPO approval
 - August-October 2015: We received IRB approval at UNCG first (submitted: 9/14/2016, received: 10/06/2015) and then used the UNCG approved IRB as the master IRB template for Temple site (submitted: 10/2015, approval: 02/26/2015). HRPO approval was sought only after a necessary app upgrade (Version 2, see below).
- **October 2015-December 2015:** Work on Major Task 3 and further protocol pilot testing/protocol improvements were completed during this time
 - The SOW for Major Task 3 only included data from 25 healthy military personnel. However, we were able to analyze data from 90 healthy military personnel during this time and we reported those data in a recent manuscript that is currently under review. Our accomplishments under Major Task 3 are detailed in a manuscript that is current under review (Appendix A) and are also outlined below.
 - The original intent of Major Task 3 was to get baseline data from healthy military personnel to be used as normative data in our app.
 - However, we were able to pair up with a research team that was examining neurocognitive changes from low level blast (LLB) exposure. Their study design included testing 4 times: baseline (prior to LLB exposure), directly after LLB exposure (POST-1), 24 hours after LLB exposure (POST-2), and 72-96 hours after LLB exposure (POST-3).
 - The original plan was just to have the participants perform our neuromotor (stepping-in-place) test at baseline to get our normative data. However, the research team allowed our neuromotor testing to occur at all 4 time points, significantly strengthening our dataset.
 - Since neurocognitive testing is a well-accepted method to identify performance decline after head perturbations, our primary question was whether neuromotor performance decline was also present in this population. If so, this finding would have important medical care considerations.
 - This was examined by splitting the studied population into two groups (with and without neurocognitive decline after LLB exposure) and then determining whether neuromotor decline was also present.
 - 90 healthy military personnel were recruited to participate in the study
 - From the total sample (N=90), 60 were trainees newly exposed to the heavy weapons training (as described below), 16 were control subjects who participated in the program, but did not take the heavy weapons training, and 14 were Range Safety Officers (RSOs). Our analysis only focused on the 60 trainees (26.3±3.5 years, all men).
 - Participants completed the neurocognitive and our neuromotor test 4 times: baseline (prior to LLB exposure), directly after LLB exposure (POST-1), 24 hours after LLB exposure (POST-2), and 72-96 hours after LLB exposure (POST-3). Stepping-in-place data were reduced to stride time data (Figure 1)
 - LLB exposure consisted of repetitive firing from shoulder-mounted rocket launchers such as M2CG 94mm (Carl Gustaf), M72 LAW 66mm (Light Anti-Tank Weapon), and RPG (Rocket Propelled Grenades) with varying munitions.

- LLB magnitude and impulse were measured via pressure sensors and were very low (5.43 and 7.14 PSI at the anterior and posterior of the head, respectively), which is only slightly above the recommended safety standard of 4 PSI.
- Our results showed that trainees with identified neurocognitive decline after LLB exposure performed the stepping-in-place task slower and with a higher level of variability in stride time immediately after exposure to LLB compared to trainees without neurocognitive decline (Figure 2).
- While both groups became faster and less variable on the stepping-in-place task as a function of repeated neuromotor testing, the relative divergence of performance immediately after LLB exposure suggests that neuromotor function can decline similarly with the neurocognitive performance after repeated sub-clinical head perturbations.
- This suggests that neurological dysfunction affects multiple domains of performance, which should be taken into account when deciding on appropriate medical care.
- It is especially important to note that all participants in this study were exposed to sub-concussive LLB, adding to a growing body of research showing that repeated subclinical head trauma can affect neurological functioning.
- Figure 1: (A) Stepping-in-place task used for neuromotor testing. The last frame in the movement sequence shows the coordinate system of the phone with the AccWalker app in the sagittal plane. In the majority of trials, phone was placed on the thigh (as depicted in the figure). In a subset of trials (~10%), it was placed on the shank midway between the ankle and the knee, but this did not affect stride time estimation (see Methods); (B) Study design (POST-2 was only completed by participants with detected neurocognitive decline); (C) Relation between the knee angle recorded via motion capture and thigh acceleration/velocity recorded by the AccWalker app; only acceleration was recorded by the phone in this study; (D) Velocity was derived from recorded acceleration via integration (see Methods). Stride time was defined based on velocity minima (peak velocity during leg return to stance); (E) Time series of the step period as a function of step number within a single 120 s trial.



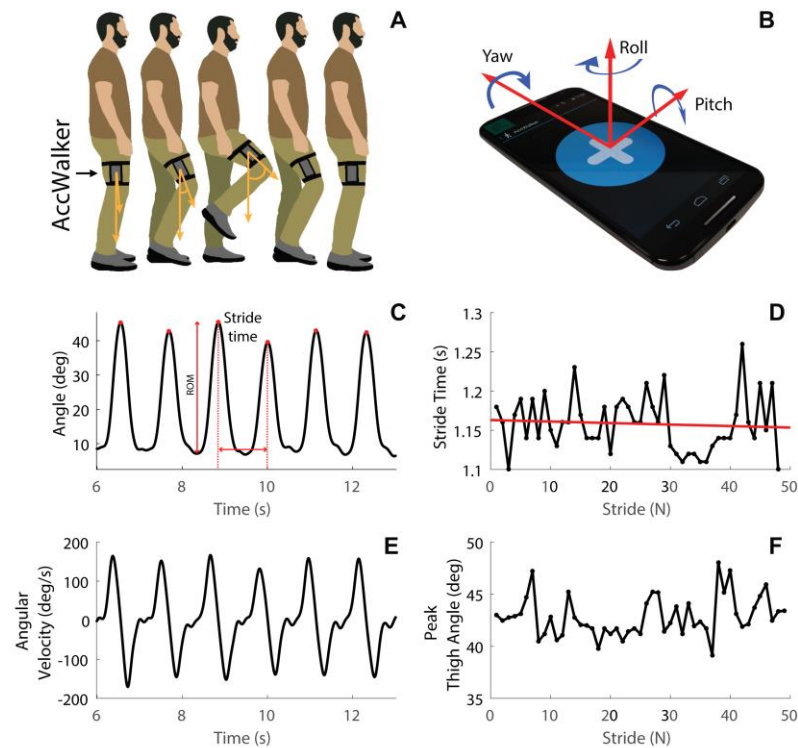
- Figure 2: Changes in the movement timing parameters by group (neurocognitive decline vs. no neurocognitive decline) as a function of blast exposure. Error bars depict standard error of the mean. Cohen's d are indicated for each between group comparison, with asterisk denoting statistically significant difference between the groups. Due to missing or unusable data, the *n* varies by time point and condition, which is represented by the number next to each data point.



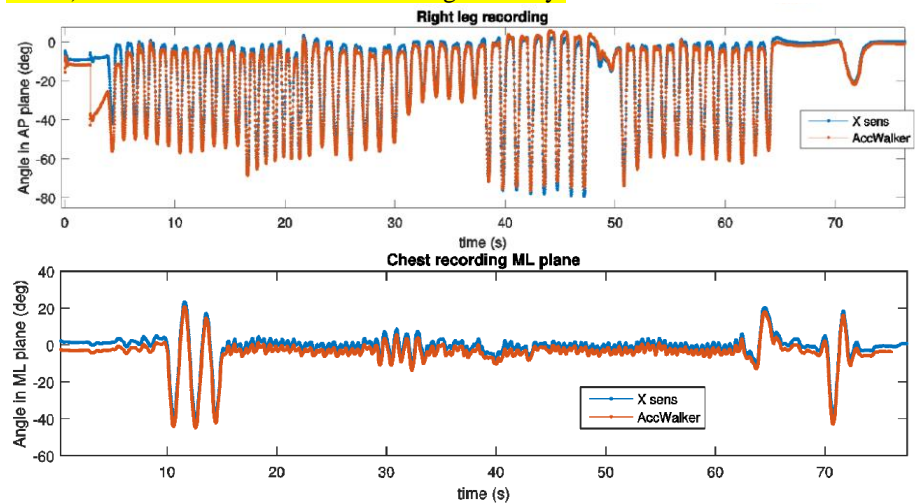
- Although the data from the 90 healthy military personnel were usable, they were not optimal. Issues with acceleration profile saturation in the smartphone app were observed in the data (see Major Task 3 below for explanation) and were replicated in further pilot testing at UNCG (see Appendix B for details)
 - Force of stepping, rate of stepping, and vertical foot displacement are all found to be factors that affect acceleration of the leg, so modifications were made (Appendix C) and tested (Appendix D), which are briefly outlined below:
 - Pilot tested different phone placements (thigh, shank, torso; Figure 3 below)



- Incorporated a pacing metronome and explicit instructions on stepping patterns
 - Incorporated orientation sensor to detect leg movement and angle (Version 2 of app, Figure 4 below)



- Tested orientation sensor detection accuracy in AccWalker compared to Xsens (research grade orientation sensor) for both thigh and torso placement (Figure 5 below). AccWalker was found to have high validity.



- Added three conditions (eyes closed (EO), eyes closed (EC), and lateral head movement (LHM) to the stepping-in-place task; analyzed pilot within- and between-day variability of acceleration and orientation profiles, consistency of phone placement, and protocol (Appendix D).

- Added the Community Balance & Mobility Scale (CB&M) to have a comparable dynamic gait task

○ **December 2015-April 2016:** Reliability and validity studies of AccWalker app Version 2

- Given the necessary changes to the app, it was imperative to complete reliability and validity measures before implementing the app in data collection (Appendix E).
 - The ICCs for a variety of stride time variables are presented in Figure 6 below. Clinically acceptable values were taken at > 0.7, indicated by the green boxes. The “Y” or “N” indicates the presence (or not) of a learning effect. AccWalker was found to have high reliability for a subset of variables. These variables will be used moving forward.

3 trials			Leg																					
ICC(2,k)	Accuracy		Period Mean		Period SD		Period CV		ACF1		Absolute TimingDrift		Drift		ThighFlex SD		Velocity Min SD		Velocity Max SD		Floquet	Moveme nt Range		
EO	0.78	Y	0.78	Y	0.80	N	0.78	N	0.44	Y	0.23	N	0.57	N	0.82	N	0.82	N	0.90	N	0.28	Y	0.91	N
EC	0.78	N	0.78	N	0.82	N	0.83	N	0.77	N	0.48	N	0.59	N	0.74	Y	0.83	N	0.85	Y	0.56	N	0.93	N
LHM	0.80	N	0.80	N	0.83	N	0.80	N	0.41	N	0.61	N	0.24	Y	0.83	Y	0.84	Y	0.88	Y	0.74	N	0.94	N

- Continued delays in IRB and HRPO approval (due to FDA issue, outlined below in Section 5, Changes/Problems) allowed for this to be completed before recruitment could begin.
- Reliability/validity results of AccWalker app Version 2 are included in a manuscript draft (Appendix F)

• **Pre-task – Institutional Review Board and Human Research Protection Office Application, timeline: 1-2 months**

○ UNCG:

- Initial IRB approval was received on: 10/06/2015
- Subsequent modifications were submitted and approved on: 12/16/2015, 02/29/2016, 05/04/2016
- HRPO Submission: 01/28/2016, Returned requesting modifications: 02/17/2016, Resubmitted on: 02/29/2016, Approval received: 04/22/2016

○ Temple:

- Initial IRB approval was received on: 02/26/2016 (submitted October 2015)
- Final modification submitted on: 05/04/2016 (currently under review)
- HRPO Submission: 02/29/2016, Approval received: 04/22/2016

○ NICoE:

- Contacted to Paula (Nikki) Kodosky to coordinate IRB approval and data collection at NICoE and was connected with COL Geoffrey Grammer, Department Chief of Research at the site on 09/03/2015
- Update: COL Grammer is no longer at NICoE, but we have been put in touch with Dr. Louis French (COL Grammer’s replacement) to start the NICoE IRB process on 05/27/2016

• **Major Task 1 – Normative data collection on healthy civilians, timeline: 3-9 months**

○ **Milestone:** 100 healthy civilians will complete the TARGET, MACE, NeuroCom’s SOT, and the Balance

- With large and accessible university populations, we do not anticipate any further difficulty with healthy civilian recruitment now that IRB and HRPO approval has been received.
- UNCG: Study recruitment begun: 04/25/2016, 10 subjects scheduled for testing in May and June
- Temple: Study recruitment begun: 04/25/2016

• **Major Task 2 – mTBI data collection on civilians, timeline: 3-9 months**

○ **Milestone:** 50 civilians with mTBI will complete the TARGET, MACE, NeuroCom’s SOT, and BESS

- UNCG: We have reached out to local orthopedic offices, athletic training department, the campus health center asking to distribute our recruitment literature to those coming in with a suspected concussion
- Temple: We have reached out to orthopedic offices, medical school/hospital, athletic training, and campus health center asking to distribute our recruitment literature to those coming in with a suspected concussion

• **Major Task 3 – Derive normative military values from previously collected data, timeline: 9-15 months**

○ **Milestone:** data from 25 healthy military personnel who previously completed the TARGET for a separate project will be analyzed to derive military-specific norm references for reliable change index calculations

- **From a February 27, 2016 email from Dr. Rhea (PI) to Dr. Tian Wang (Scientific Officer):** “We had the opportunity to analyze data on more military personnel than original proposed. A total of 90 military personnel completed our task using version 1 of our app. Further, we not only collected normative data prior to low-level blast (LLB) exposure, we were also able to collect data right after LLB exposure, 24 hours post-exposure, and 72 hours post-exposure. Data from Major Task 3 are presented in a manuscript currently under review at the *Journal of Military Medicine*. Lessons learned for Major Task 3 led us to slightly modify the protocol and our app. Version 2 of our app has been developed and the reliability and validity, which were already established for version 1, are now being established in my lab and will result in our next publication. Further, our DARPA funded colleagues who gave us access to the first 90 military personnel (Navy SEALs) in our study have agreed to include our updated app and protocol in their next round of testing, which will include Marine Breachers (a

second group exposed to LLB). We will again get data before, directly after, 24 hours after, and 72 hours after LLB exposure. Although this follow-up study is outside the scope of Major Task 3, we want to report on how we are continuing to move forward the science with respect to our funded project.”

- Data from Major Task 3 (reported in the manuscript referenced above) is attached (Appendix A). Data collection from the Marine Breacher study is slated to start in July 2016 and will be compared to the SEAL data for replication purposes.

- **Major Task 4 – mTBI data collection on military personnel, timeline: 15-21 months**

- **Milestone:** 25 military personnel with mTBI from NICoE will complete the TARGET to determine the clinical utility of the TARGET as an mTBI screen in military populations
- **From a February 27, 2016 email from Dr. Rhea (PI) to Dr. Tian Wang (Scientific Officer):** “The original intent of Major Task 4 was to use our app (informed by data derived from Major Tasks 1-3) to collect data on those with mTBI symptoms in the chronic phase from NICoE to determine the sensitivity and specificity of our protocol and app. While we intend on fulfilling our commitment to Major Task 4, we have also been able to collect acute mTBI data with our N = 90 Navy SEALs in Major Task 3 (approximately 1/3 had concussion symptoms after LLB exposure), and we will be able to do the same with the upcoming Marine Breacher study. Thus, we will again be able to go above and beyond by gathering data in both the acute and chronic phases of mTBI to better determine the sensitivity and specificity of our app. We understand the extra data collection in Major Tasks 3 & 4 are outside the scope of the funding your office provided. However, we are confident that we will be able to not only deliver on the Tasks listed in our SOW, but also gather and analyze the extra data without asking for extra funding, which will provide a stronger return-on-investment to you and your Office.”
- Data from Major Task 3 is attached (Appendix A). Data collection from the Marine Breacher study is slated to start in July 2016 and the mTBI data will be compared to the SEAL data for replication purposes.

- **Major Task 5 – data analysis/software optimization, timeline: 17-24 months**

- This task cannot be completed until Tasks 1-4 are completed.

- **Additional accomplishments/comments:**

- FITBIR account created and orientation conference call occurred on 05/27/2016
- Most recent study protocol and assessment descriptions included in Appendix G

What do you plan to do during the next reporting period to accomplish the goals?

If this is the final report, state “Nothing to Report.”

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

- Major Task 1: Heavy recruitment from the two university campuses (UNCG and Temple) and surrounding city areas will allow for quick completion of the healthy civilian data set
- Major Task 2: Approaching multiple clinical sites for potential mTBI subjects will allow for efficient recruitment of the mTBI population. Access to student health centers, athletic programs, and a medical school (Temple) will aide this process.
- Major Task 3: Though completed, data collection on a Marine Breacher cohort (outside our SOW) will start
- Major Task 4: Coordination with NICOE for the submission of IRB and HRPO paperwork has begun and should move quickly since approval has been received at the other sites
- Major Task 5: Once Tasks 1-4 are completed, analysis and optimization can be completed

4. IMPACT: Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

What was the impact on the development of the principal discipline(s) of the project?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

The findings/results/techniques from this project are still in the data collection phase, so we cannot state how they have made an impact yet. However, we can speculate as to their potential impact. The goal of this project is to provide a portable, objective assessment of balance using an Android-based smartphone app that can assist in the screening after a suspected mTBI. Our initial data (Appendix A) showed that our app was able to pick up on balance dysfunction after low-level blast exposure in a military population. While promising, that data was not optimal (Appendix B), so we recently developed Version 2 of the app (Appendices C-F), which will be used in all data collections moving forward (Appendix G). If successful, our app could have a large impact on the principle discipline (concussion detection) by providing an easy to use and cost effective means to measure balance dysfunction.

What was the impact on other disciplines?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

In addition to helping the military with concussion detection, it is plausible that our app could be used in other settings, such as sport-related concussion detection (i.e., sideline testing) or detection of balance dysfunction in a roadside test of a person suspected of driving under the influence.

What was the impact on technology transfer?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

What was the impact on society beyond science and technology?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

- 5. CHANGES/PROBLEMS:** The Project Director/Principal Investigator (PD/PI) is reminded that the recipient organization is required to obtain prior written approval from the awarding agency Grants Officer whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:

Changes in approach and reasons for change

Describe any changes in approach during the reporting period and reasons for these changes.

Remember that significant changes in objectives and scope require prior approval of the agency.

- AccWalker/TARGET protocol:
 - CHANGE: Included orientation sensor to determine thigh angle during stepping-in-place task
 - REASON: Phone orientation and thigh angle were deemed necessary metrics given the issues with acceleration profile saturation listed above in the accomplishments section
 - CHANGE: Reduced stepping-in-place task time to 70 seconds
 - REASON: A shorter stepping-in-place task was deemed sufficient for the analyses we will run and cuts down on potential fatigue interference in the mTBI populations
 - CHANGE: Included three conditions for the task: eyes open, eyes closed, and head rotation conditions
 - REASON: Additional tasks were added in order to further tax the neurological system, thus creating a measure that further distinguishes healthy from concussed individuals
- CHANGE: Removed the second Balance Error Scoring System (BESS) test and included a filming portion
 - REASON: Second BESS test removed to reduce study visit time
 - REASON: Filming added to accurately check errors during the assessment
- CHANGE: Included the Community Balance and Mobility (CB&M) scale
 - REASON: Deemed it necessary to have comparable dynamic balance and mobility task

Actual or anticipated problems or delays and actions or plans to resolve them

Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

- Delay in research staff hires postponed IRB and HRPO submissions by 4 months
- Questions regarding device status as it pertains to the FDA arose at Temple, delaying IRB and HRPO approval by 4 months, issue has been resolved and is detailed below:
 - **From a February 27, 2016 email from Dr. Rhea (PI) to Dr. Tian Wang (Scientific Officer)**
“As soon as we found out we received funding for this project, we had conversations with the UNCG IRB and the UNCG Office of Innovation Commercialization (OIC), the latter of which is responsible for making institutional level decision about the need for FDA approval. Both the IRB and OIC agreed that our app was only a data collection device at this time and not to be used for medical screening. Although medial screening is the intention down the road, both offices agreed our app at this time did not require an FDA IDE based on the February 9, 2015 DHHS issuance "Mobile Medical Applications: Guidance for Food and Drug Administration Staff". Thus, the UNCG IRB approved our application without the need for an FDA IDE. Once we had UNCG IRB approval, Temple submitted their IRB application and it was deferred partially based on the FDA issue. I then wrote a support letter highlighting why UNCG did not require an FDA IDE and cited specific text in the February 9, 2015 DHHS issuance to support our position). The Temple IRB agreed with our position and they approved our protocol on February 26, 2016 without needing an FDA IDE. Thus, we hope this explains the FDA issue and why that challenge is no longer an issue.”
- The need to include an orientation sensor in the most recent app version delayed collection as reliability studies were necessary before actual study collection could begin (Appendices B-F)

Changes that had a significant impact on expenditures

Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

- As stated above, staff hires (project coordinator and post-doc) were delayed, resulting in reduced expenditures for May, June, July, and part of August

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

- As stated above, the only changes to human subject protocols were the addition of a filming portion to the BESS assessment and the addition of eyes closed and head rotation conditions to the TARGET protocol
- IRB and HRPO approval:
 - UNCG:
 - Initial IRB approval was received on: 10/06/016
 - Subsequent modifications were submitted and approved on: 12/16/2015, 02/29/2016, 05/04/2016
 - HRPO Submission: 01/28/2016, Returned requesting modifications: 02/17/2016, Resubmitted on: 02/29/2016, Approval received: 04/22/2016
 - Temple:
 - Initial IRB approval was received on: 02/26/2016 (submitted November 2015)
 - Final modification submitted: 05/04/2016 (waiting for approval)
 - HRPO Submission: 02/29/2016, Approval received: 04/22/2016

Significant changes in use of biohazards and/or select agents

Not applicable

6. PRODUCTS: List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”

- **Publications, conference papers, and presentations**
Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume; year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Rhea CK, Kuznetsov NA, Bailie JM, Yanagi MA, Long B, Haran FJ, Ross SE, Wright WG, Robins RK, Jakiela JT, Sargent PD, Duckworth JL. “Development of a portable tool for screening neuromotor sequelae from repetitive low-level blast exposure.” *Journal of Military Medicine* (submitted; federal support acknowledged) (Appendix A)
We received favorable reviews on July 6th. We have revised our manuscript based on those reviews and will be resubmit our paper on July 27th. Appendix A has been updated with the revised manuscript.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: Author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Other publications, conference papers, and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

*Rhea, C.K., Haran, F.J., Ross, S.E., Yanagi, M.A., Bailie, J.M., Sargent, P.D., & Duckworth, J.L. Evaluation of neuromotor function following blast exposure. *Military Health System Research Symposium*, Fort Lauderdale, FL, August, 2015, national conference, poster. (Appendix H)

Rhea, C.K., Kuznetsov, N.A., Long, B., MacPherson, R.P., Jakiela, J.T., Robins, R.K., Haran, F.J., Ross, S.E., & Wright, W.G. Can a smartphone app be used to objectively measure neuromotor control after a concussion? North American Society for the Psychology of Sport and Physical Activity, Montreal, Quebec, June 2016, national conference, podium. (Appendix I)

Kuznetsov, N. A., Cone, B., Schleich, K.N., Hege, M.A., Ross, S.E., Long, B., Robins, R.K., Wright, W.G., Haran, F.J. & Rhea, C.K. Reliability of movement timing metrics provided by a portable gait assessment protocol. North American Society for the Psychology of Sport and Physical Activity, Montreal, Quebec, June 2016, national conference, podium. (Appendix J)

*Rhea, C.K., Kuznetsov, N.A., Bailie, J.M., Yanagi, M.A., Long, B., Haran, F.J., Ross, S.E., Wright, W.G., Robins, R.K., Jakiela, J.T., Sargent, P.D., & Duckworth, J.L. Concussion history influences neuromotor performance after exposure to repetitive low-level blast exposure. American Society of Biomechanics, Raleigh, NC, August 2016, national conference. (Appendix K)

Kuznetsov, N.A., Robins, R.K., Ross, S.E., Wright, W.G., Haran, F.J., Jakiela, J.T., Bailie, J.M., Yanagi, M.A., Long, B., Duckworth, J.L., & Rhea, C.K. Neuromotor testing post-mTBI: Reliability of movement metrics from a smartphone application. Military Health System Research Symposium, Kissimmee, FL, August, 2016, national conference, under review. (Appendix L)

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. In addition to a description of the technologies or techniques, describe how they will be shared.

As stated previously, the AccWalker app now includes a pacing metronome and orientation sensor, necessary changes implemented after Major Task 3 analysis. The TARGET protocol now includes eyes closed and head rotation conditions and is only 70 seconds in length.

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. State whether an application is provisional or non-provisional and indicate the application number. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment, and/or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *biospecimen collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change.”

Example:

*Name: Mary Smith
Project Role: Graduate Student
Researcher Identifier (e.g. ORCID ID): 1234567
Nearest person month worked: 5*

Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.

Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award).

Name:	Christopher Rhea (UNCG)
Project Role:	PI
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	2
Contribution to Project:	Lead of the study, developed protocol and analyses, oversees data collection/processing/analysis
Name:	Scott Ross (UNCG)
Project Role:	Co-Investigator
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	1
Contribution to Project:	Oversees data collection/processing/analysis, responsible for assessment training (BESS)
Name:	Nikita Kuznetsov (UNCG)
Project Role:	Post Doc
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	9
Contribution to Project:	Primary data collector/analyst, conducted reliability and validity studies on versions 1 and 2 of AccWalker, assisted in protocol modification
Name:	Jason Jakiela (UNCG)
Project Role:	Project Coordinator
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	9
Contribution to Project:	Oversees the day to day of the study, prepares study documentation, assists in protocol modification and data collection/analysis

Name:	Ben Long (UNCG)
Project Role:	AccWalker Developer/Consultant
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	1
Contribution to Project:	Application development and updating
Name:	Geoff Wright
Project Role:	Co-Investigator (Temple)
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	1
Contribution to Project:	Leads study from Temple site, developed protocol and analyses, oversees data collection/processing/analysis
Name:	Becca Robins
Project Role:	Post Doc (Temple)
Researcher Identifier (e.g. ORCID ID):	n/a
Nearest person month worked:	7
Contribution to Project:	Primary data collector/analyst for Temple site, contributed to reliability/validity collection and analysis of AccWalker

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to report

What other organizations were involved as partners?

If there is nothing significant to report during this reporting period, state “Nothing to Report.”

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:

Organization Name:

Location of Organization: (if foreign location list country)

Partner’s contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner’s facilities for project activities);*
- *Collaboration (e.g., partner’s staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner’s staff use each other’s facilities, work at each other’s site); and*
- *Other.*

- Organization: Temple University
 - Location: Philadelphia, PA
 - Contributions: collaboration
 - Data collection is concurrent with the Temple site for the civilian populations
- Organization: NICOE
 - Location: Bethesda, MD
 - Contributions: collaboration
 - Data collection for the military populations will be conducted at this site
- Organization: Uniformed Services University of the Health Sciences
 - Location: Bethesda, MD
 - Contributions: collaboration
 - Collected AccWalker data outlined in Major Task 3 were obtained from CDR Josh Duckworth via a DARPA funded project at the Uniformed Services University of the Health Sciences

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: For collaborative awards, independent reports are required from BOTH the Initiating PI and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.

QUAD CHARTS: If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.

9. **APPENDICES:** Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.

Appendix A

Manuscript currently under review at the *Journal of Military Medicine* from data derived from Major Task 3 of this award (revised version submitted with this report)

Appendix B

Data analysis from Major Task 3 of this award, along with a highlight of the challenges with these data

Appendix C

TARGET protocol modifications due to challenges highlighted in Appendix B

Appendix D

Pilot data of TARGET protocol modifications proposed in Appendix C

Appendix E

Reliability and validity of modified TARGET protocol outlined in Appendix D

Appendix F

Manuscript draft of the reliability and validity data from the modified TARGET protocol described in Appendix E

Appendix G

Up-to-date study protocol and assessments

Appendix H

Abstract presented at the 2015 Military Health System Research Symposium

Rhea, C.K., Haran, F.J., Ross, S.E., Yanagi, M.A., Bailie, J.M., Sargent, P.D., & Duckworth, J.L. Evaluation of neuromotor function following blast exposure. *Military Health System Research Symposium*, Fort Lauderdale, FL, August, 2015, national conference, poster.

Appendix I

Abstract to be presented at the 2016 North American Society for Psychology of Sport and Physical Activity conference

Rhea, C.K., Kuznetsov, N.A., Long, B., MacPherson, R.P., Jakiela, J.T., Robins, R.K., Haran, F.J., Ross, S.E., & Wright, W.G. Can a smartphone app be used to objectively measure neuromotor control after a concussion? North American Society for the Psychology of Sport and Physical Activity, Montreal, Quebec, June 2016, national conference, podium.

Appendix J

Abstract to be presented at the 2016 North American Society for Psychology of Sport and Physical Activity conference

Kuznetsov, N. A., Cone, B., Schleich, K.N., Hege, M.A., Ross, S.E., Long, B., Robins, R.K., Wright, W.G., Haran, F.J. & Rhea, C.K. Reliability of movement timing metrics provided by a portable gait assessment protocol. North American Society for the Psychology of Sport and Physical Activity, Montreal, Quebec, June 2016, national conference, podium.

Appendix K

Abstract to be presented at the 2016 American Society for Biomechanics conference

Rhea, C.K., Kuznetsov, N.A., Bailie, J.M., Yanagi, M.A., Long, B., Haran, F.J., Ross, S.E., Wright, W.G., Robins, R.K., Jakiela, J.T., Sargent, P.D., & Duckworth, J.L. Concussion history influences neuromotor performance after exposure to repetitive low-level blast exposure. American Society of Biomechanics, Raleigh, NC, August 2016, national conference.

Appendix L

Abstract to be presented at the 2016 Military Health System Research Symposium

Kuznetsov, N.A., Robins, R.K., Ross, S.E., Wright, W.G., Haran, F.J., Jakiela, J.T., Bailie, J.M., Yanagi, M.A., Long, B., Duckworth, J.L., & Rhea, C.K. Neuromotor testing post-mTBI: Reliability of movement metrics from a smartphone application. Military Health System Research Symposium, Kissimmee, FL, August, 2016, national conference, under review